Debate & Analysis

Lower urinary tract symptoms and prostate cancer:

is PSA testing in men with symptoms wise?

INTRODUCTION

The best evidence to date shows that, overall, the harms of prostate cancer screening in asymptomatic men outweigh the benefits. A 2013 Cochrane review found that screening asymptomatic men did not save lives from the disease, and leads to detection of indolent prostate cancers that would not have gone on to cause harm in a man's lifetime.[1] This is known as overdiagnosis. Further weight was added to the results of the Cochrane review in the recent 10-year follow-up results from the cluster randomised trial of PSA testing for prostate cancer (CAP), which found that one-off PSA testing of asymptomatic men did not save lives from prostate cancer.[2]

For symptomatic men, however, the clinical situation is different. Current clinical guidelines from the National Institute for Health and Care Excellence (NICE) recommend that GPs consider a PSA test and digital rectal examination (DRE) in men presenting with lower urinary tract symptoms (LUTS) to investigate suspected prostate cancer.[3]

For the purposes of this article we defined LUTS as: nocturia, urgency, frequency, incomplete voiding, intermittency, terminal dribble, hesitancy, straining, weak or split stream, and/or post-micturation dribble. LUTS are very common in men, and have been estimated to be present in around 80% of men aged >60 years.[4]

The 2013 Cochrane review stated that *'... the presence of LUTS, typically due to benign prostatic obstruction, are very common in the ageing male and are not considered to increase prostate cancer risk. Therefore, PSA testing or DRE in men with LUTS is also considered screening.'*[1] Because of their high prevalence, giving men with LUTS a PSA test may carry the same harms as PSA screening; however, there is not a clear consensus on this issue.

This article reviews the evidence for a link between LUTS and prostate cancer, and asks whether using the PSA test to investigate men with LUTS is clinically appropriate.

CURRENT CLINICAL GUIDANCE

NICE guidance recommends that GPs consider a PSA test and DRE to investigate suspected prostate cancer in men presenting with erectile dysfunction, visible haematuria, or any LUTS.[3]

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These recommendations are based primarily on findings from a 2006 English case–control study, which identified presenting symptoms in men diagnosed with prostate cancer.[5] This study has many strengths, including being representative of primary care presentation. However, it also has several limitations (which are common to primary care research). It is a small study and does not include mortality or stage data. As a result, it is not possible to know if these symptoms are linked to clinically significant prostate cancer, rather than overdiagnosed cases.

LUTS AND PROSTATE CANCER: WHAT IS THE EVIDENCE?

Our evidence search identified three other key studies that investigated the link between LUTS and prostate cancer.

The first is a 2008 UK-based case–control study nested within the Prostate testing for cancer and Treatment study (ProtecT), involving over 65 000 men.[6] Men from the general population aged 50–69 years were invited for a PSA test, and at the same time presence of LUTS (frequency, nocturia, urgency, leakage, and hesitancy) and symptom severity were ascertained by questionnaire. Men with a PSA ≥3 ng/mL were subsequently invited for biopsy.

When adjusted for age, PSA level, and family history of prostate cancer, no link between LUTS and an increased risk of prostate cancer was found.

The second study is a Norwegian cohort study of 21 000 men, HUNT2.[7] Participants were recruited from the general population and had the presence and severity of LUTS assessed at baseline by questionnaire, and were followed up for 9 years. LUTS were associated with an increased risk of localised prostate cancer. However, there was no link between LUTS of any severity and advanced prostate cancer (defined as the presence of regional or distant metastases at diagnosis), nor prostate cancer-specific mortality.

The third study is QCancer®, a large UK-based cohort study involving EMIS data from 676 GP practices. Three LUTS were found to be significantly predictive of prostate cancer: urinary retention, frequency, and nocturia.

ProtecT suggests that the absence of LUTS in men with raised PSA levels is linked to prostate cancer. HUNT2 and QCancer in comparison both found LUTS were positively associated with prostate cancer. In HUNT2, this is driven by localised cases (a proportion of which are likely to be overdiagnosed). It is unclear if this is also true for QCancer, as it did not report stage or mortality data. Overall, these studies suggest LUTS increase the risk of a prostate cancer diagnosis but do not show that LUTS are predictive of advanced or non-indolent disease.

Additionally, most prostate cancers arise in the peripheral zone of the prostate, and, as other researchers point out, for LUTS to be caused by prostate cancer it is reasonable to assume it would be advanced.[7]

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IMPLICATIONS FOR GENERAL PRACTICE

The potential implications of these findings for general practice are complex, given PSA testing extends beyond the investigation of prostate cancer.

The PSA test can also be used to investigate men with suspected benign prostatic hyperplasia (BPH).[8] But if elevated above the age-specific reference range, as might be expected in a man with this condition, the next step when following NICE clinical guidance is to *'refer men using a suspected cancer pathway referral …'*.[3] This leaves clinicians in a grey area: wanting to effectively investigate their patients' symptoms, but without providing 'Too Much Medicine'[9] and putting patients at risk of overdiagnosis and overtreatment.

NEXT STEPS

Although HUNT2 and ProtecT are both robust, it is not clear if their findings can be extrapolated to primary care. It is likely that men presenting to their GP and reporting LUTS unprompted are inherently different from study participants where symptoms are obtained by questionnaire.

QCancer provides large, real-world data on LUTS and prostate cancer; however, it is limited by the lack of data on prostate cancer stage and mortality. This remains an area needing further primary care research.

Due to this uncertainty, and in the absence of a better test, a prudent action may be for GPs to have an informed-choice discussion with their symptomatic patients about the test's harms and benefits.

Of course, until these harms and benefits are better quantified, it may be difficult to have an impactful discussion. But it is currently possible to inform patients that:

- early prostate cancer is unlikely to have any symptoms, and in most cases LUTS will be due to causes other than prostate cancer; and
- PSA testing to investigate LUTS, whatever the cause, may lead to detection of a prostate cancer that would not have gone on to cause harm. This may lead to overtreatment, potential side effects, and psychological distress.

CONCLUSION

The benefit-to-harm ratio of using PSA to investigate men with LUTS is unclear, but research to date suggests that this practice places men at risk of overdiagnosis.

Until there are clearer answers, and in the absence of an alternative to PSA testing, a wise step may be that GPs, once they have considered a PSA test to be necessary, have a discussion with their symptomatic patients so that they are aware of the harms and benefits.

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